UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,734	10/08/2003	David M. Goldenberg	40923-0051US5	5299

35657 7590 01/11/2007

FAEGRE & BENSON LLP
PATENT DOCKETING
2200 WELLS FARGO CENTER
90 SOUTH SEVENTH STREET
MINNEAPOLIS, MN 55402-3901

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

PTOL-90A (Rev. 10/06)

Office Action Summary	**Application No.** 10/680,734	**Applicant(s)** GOLDENBERG ET AL.
	Examiner Lynn Bristol	**Art Unit** 1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,10,11,44,49-51,55 and 108* is/are pending in the application.
4a) Of the above claim(s) *44,49-51 and 55* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1,6,7,10,11 and 108* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/27/06 has been entered.

2. Claims 12-43, 45-48, 52-54 and 56-107 were cancelled and claims 44, 49-51 and 55 are withdrawn in the Response of 11/27/06.

3. Claims 1, 6, 7, 44 and 49-51 and 55 were amended in the Response of 11/27/06.

a) Claims 1, 6, 7, 44 and 49-51 were amended to delete the phrase "or fragment thereof".

b) Claim 1 has been amended to recite a dosage range of "100 to 600".

c) Claims 6 and 49 have been amended to delete the limitation that the light and heavy chain CDR1-3 "comprise the amino acid" of the respective SEQ ID NO.

d) Claim 6 has been amended to recite that the light and heavy chain CDR1-3 are from murine MN-14 antibody.

e) Claim 44 has been amended to depend from Claim 1 and to recite "at least one naked anti-CEA monoclonal antibody."

f) Claim 55 has been amended to delete the non-elected species of therapeutic agent.

4. Claims 1, 6, 7, 10, 11, 44, 49-51, 55 and 108 are all the pending claims for this application.

5. Claims 1, 6, 7, 10, 11 and 108 are all the claims under examination.

6. Applicants amendments to the claims have necessitated new grounds for rejection. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

35 USC § 112-first paragraph, new matter

7. The rejection of Claims 9, 12 and 15 under 35 U.S.C. 112, first paragraph, for lack of written description support is withdrawn. The rejection of Claims 9, 12 and 15 is rendered moot in view of cancellation of the claims.

35 USC § 103(a)

8. The rejection of Claims 1, 9-11 and 15 under 35 U.S.C. 103(a) as being unpatentable over Primus et al. (USPN 4,818,709) as evidenced by Hansen et al. (Cancer 71:3478-85 (1993)) and in view of Carter et al. (US 20050222392) is withdrawn. The rejection of Claims 9 and 15 is rendered moot in view the cancelled claims. With respect to Claims 1, 10 and 11, the Examiner has considered Applicants comments set forth on p. 6, ¶2- p. 7, ¶4 of the Response of 11/27/06, and the arguments with respect to Primus and Carter are found persuasive. Primus does not teach a humanized anti-CEA antibody combined in a formulation with a therapeutic

agent and the sequential or concurrent administration. However, by incorporation of reference to USPN 4,331,647 (Col. 19, lines 38-44), Primus discloses administering a dose of antibody greater than 100 mg. As Applicants correctly point out, the 102(e) date of Carter is the PCT filing date (April 7, 2003).

Applicants' comments regarding Hansen are not persuasive in view of element (i) of Claim 1. Hansen specifically teaches the Class III, anti-CEA Mab, MN-14, thus it is unclear how Applicants have concluded that Hansen is irrelevant to the claims. Nevertheless, because Hansen does not stand alone as a prior art reference against the claims or rectify the deficiencies of Primus, the rejection is withdrawn.

9. The rejection of Claim 1 under 35 U.S.C. 103(a) as being unpatentable over Primus et al. (USPN 4,818,709) in view of Carter et al. (US 20050222392) and Queen et al. (5,530,101) is withdrawn. Applicant's arguments filed on p. 6, ¶2- p. 7, ¶4 of the Response of 11/27/06, are found persuasive. However, upon further consideration, a new ground(s) of rejection is made in view of Primus et al. (USPN 4,818,709) in view of Queen et al. (5,530,101).

10. The rejection of Claims 1, 6, 10, 11 and 108 under 35 U.S.C. 103(a) as being unpatentable over Hansen (USPN 5,874,540), Griffiths et al. (USPN 7011812) and Govindan et al. (US20040001825) is withdrawn.

Applicant's arguments, see p. 7, ¶5- p. 8, ¶1, filed in the Response of 11/27/06, with respect to the rejection(s) of claim(s) 1, 6, 10, 11 and 108 under the combined references have been fully considered and are persuasive. Applicants' arguments against Hansen were cited in the previous Response of 8/21/06. Applicants have met the conditions under 35 U.S.C. 103(c) in disqualifying the Griffiths et al. (USPN 7011812) and Govindan et al. (US20040001825) references as prior art under 35 U.S.C. 103(a) by asserting that the references were at the time of invention was made, ownded by or subject to an obligation of assignment to the same person.

However, upon further consideration, a new ground(s) of rejection is made in view of Hansen (USPN 5,874,540), Griffiths et al. (USPN 7011812) and Govindan et al. (US20040001825) as set forth infra.

Rejections Maintained

35 USC § 112-first paragraph, new matter

11. The rejection of Claims 1, 6, 7, 10, 11 and 108 under 35 U.S.C. 112, first paragraph, for lack of written description support is maintained. Applicant's arguments filed on p, 6, ¶1 of the Response of 11/27/06 and the amendment of Claim 1 to recite "100 to 600 mg" have been fully considered but they are not persuasive.

Applicants allege "The Action states that, "Applicants' specification describes dosage ranges for the MN-14 antibody or fragment thereof at, for example, 100 to 600 milligrams protein per dose per injection." Therefore, the Action explicitly acknowledges support for a dose range of 100 to 600 mg."

The Examiner submits that if the claims were directed to the antibody alone then the recitation "100 to 600 mg protein per dose per injection" could find support.

However, this is not the instant case. The composition claims comprise both the antibody and a therapeutic agent, and as stated in the Office Action of 10/19/06, the specification teaches antibody dose ranges "for multimodal therapy (antibody and cytotoxic agent) 0.5-15 mg/kg body weight per infusion, more preferably 2-8, and still more preferably 3-5 mg/kg per infusion [0112]." Thus the specification does not provide written description support for the composition or multimodal therapy where the naked humanized anti-CEA Mab is formulated in a dosage of 100 to 600 mg, much less that the dose is appropriate for treating cancer.

New Grounds for Rejection

35 USC § 112-second paragraph

12. Claims 1, 6, 7, 10, 11 and 108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 1, 6, 7, 10, 11 and 108 are indefinite as being drawn to a composition comprising both the antibody and therapeutic agent wherein the two components are formulated for "concurrent or sequential administration", because in Claim 1 it is not clear how the two components are required to be within the same composition yet formulated for sequential administration. The specification teaches that a "composition comprises at least one Class III anti-CEA monoclonal antibody (MAb) or fragment thereof and at least one therapeutic agent, which are not conjugated to each other, and thus are present in the composition as unconjugated forms of each of the components" [0095]. The limitation (ii) of Claim 1 where the antibody and the therapeutic agent are formulated for "sequential administration" would appear contrary to Applicants definition of a "composition", as each of the components need be administered separately.

b) Claims 1, 6, 7,.10, 11 and 108 recite the limitation "the anti-CEA MAb" in Claim 1 at (i). There is insufficient antecedent basis for this limitation in the preamble of claim 1, which is drawn to "naked anti-carcinoembryonic antigen (anti-CEA) monoclonal antibody (MAb)".

c) Claims 1, 6, 7, 10, 11 and 108 recite the limitation "said naked humanized anti-CEA MAb" in Claim 1 at (ii) and (iii). There is insufficient antecedent basis for this limitation in the preamble of claim 1, which is drawn to "naked anti-carcinoembryonic antigen (anti-CEA) monoclonal antibody (MAb)".

d) Claims 6 and 7 are indefinite for the recitations for the light chain of "CDR1 KASQDVGTSVA (SEQ ID NO: 20); CDR2 WTSTRHT (SEQ ID NO: 21); and CDR3 QQYSLYRS (SEQ ID NO: 22);" and for the heavy chain of "CDR1 TYWMS (SEQ ID NO: 23); CDR2 EIHPDSSTINYAPSLKD (SEQ ID NO: 24); and CDR3 LYFGFPWFAY (SEQ ID NO: 25)" because in Claim 6 it is not clear what the relationship is between the CDR and the corresponding peptide sequence. Amending the claim to recite, for example, "having an amino acid sequence therein of" could overcome the rejection.

35 USC § 103

13. Claims 1 (and 10) under 35 U.S.C. 103(a) are unpatentable over Primus et al. (USPN 4,818,709) in view of Queen et al. (5,530,101).

Claim 1 has been amended to recite “100 to 600 mg.” Claim 1 is indefinite for reasons discussed infra under “New Grounds for Rejection”, however, in order to advance prosecution, the claim is interpreted as being drawn to the class of humanized Class III, anti-CEA Mabs. The interpretation of Claim 10 is of record.

Applicant's arguments filed on p. 6, ¶2- p. 7, ¶4 of the Response of 11/27/06 have been fully considered but they are not persuasive. Applicants allege “The Office Action is unable to point to any disclosure in Primus... or Queen et al. that discloses the claimed subject matter.”

The Examiner resubmits and incorporates the arguments in full regarding the Primus and Queen references as discussed in section 10 of the Office Action of 5/25/06 and further as follows.

Primus discloses Class III, anti-CEA Mabs for treating cancer, and through incorporation by reference to USPN 4,331,647 (Col. 19, lines 38-44), Primus discloses administering a dose of antibody greater than 100 mg.

Queen discloses compositions containing human-like antibodies or a cocktail thereof can be administered for prophylactic and/or therapeutic treatments. Queen discloses a range from about 1 to about 200 mg of antibody per dose, with dosages of from 5 to 25 mg being more commonly used. Queen discloses the antibodies of the present invention can also be used as separately administered compositions given in conjunction with chemotherapeutic or immunosuppressive agents.

The dose range of Claim 1 falls within the dose of Primus and is overlapping with the dose of Queen for a non-humanized and humanized Class III, anti-CEA Mab, respectively. On the basis of Queen demonstrating improved results, i.e., non-specific immune response (HAMA) with the humanized antibodies, Applicants have not provided any probative evidence or sufficient arguments that suggest why at the time of the invention, one skilled in the art would have no motivation or not been assured of reasonable success in having produced a humanized Class III, anti-CEA Mab.

For all of these reasons, the rejection is maintained.

Applicants are invited to submit extrinsic evidence showing improved or unexpected results for the instant claimed composition.

14. Claims 1, 6, 7, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen et al. (Cancer 71:3478-85 (1993); "Hansen I") or Hansen et al. (USPN 5,874,540; "Hansen II") in view of Queen et al. (USPN 5,530,101).

The interpretation of Claims 1, 6, 7, 10 and 11 is discussed supra and is of record.

The claims are prima facie obvious at the time the invention was made over Hansen I in view of Hansen II and Queen.

The interpretation of Hansen I is of record. Hansen I does not disclose humanized MN-14 Mab in combination with a therapeutic agent, where the humanized MN-14 Mab has framework residues from the murine framework, or where the therapeutic agent is a cytotoxin. Hansen II and Queen rectify these deficiencies.

The interpretation of Hansen II is of record.

The interpretation of Queen is of record and the discussion reiterated supra.

One skilled in the art at the time the composition was made would have been motivated to have produced the composition in view of Hansen I, Hansen II and Queen. Hansen I discloses consistently improved targeting with MN-14 in tumor xenografts in mice and excellent specificity and sensitivity with MN-14 in a clinical phase I trial. Hansen II discloses humanized MN-14 Mab being less immunogenic and immunoconjugates with doxorubicin. Queen discloses the advantages of humanized Mabs being less immunogenic, including donor framework residues in the acceptor antibody, and dose ranges for antibodies from about 1 to about 200 mg of antibody per dose, with dosages of from 5 to 25 mg being more commonly used. Queen discloses the antibodies of the present invention can also be used as separately administered compositions given in conjunction with chemotherapeutic or immunosuppressive agents.

The motivation to obtain an improved MN-14 antibody of Hansen I based on the teachings of Hansen II and Queen for humanization effects improvement on Mabs would have provided one skilled in the art a reasonable assurance of success in producing such an antibody molecule and further in composition form with a cytotoxic agent such as doxorubicin.

For all of these reasons, the claims were prima facie obvious at the time of invention in view of Hansen I, Hansen II and Queen.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1, 6, 10, 11 and 108 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, and 10 of Griffiths et al. (U.S. Patent No. 7,001,812) in view of Hansen (USPN 5,874,540) and Govindan et al. (US20040001825).

The interpretation of Claims 1, 6, 10, 11 and 108 has been discussed supra and is of record.

The claims were prima facie obvious at the time the invention was made over claims 1, 2 and 10 of Griffiths in view of Hansen and Govindan.

Griffiths claims a composition for effecting therapy of a tumor in a patient, comprising a therapeutic naked antibody and a second therapeutic agent (Claim 1), where the therapeutic agent is a radionuclide, cytokine, drug, or toxin (Claim 2), where the drug is a nitrogen mustard, a triazene, a vinca alkaloid, and an antibiotic (Claim 10). Griffiths discloses a humanized anti-CEA antibody (MN-14) as an antibody in the composition. Griffiths discloses species for the following drugs: cyclophosphamide (nitrogen mustard), DTIC (triazene), vincristine (vinca alkaloid), doxorubicin (antibiotic) and the prodrug CPT-11 (irinotecan) (MPEP 804 "The specification can be used as a dictionary to learn the meaning of a term in the patent claims. *Toro Co. v. White Consul Indus. Inc.* 199 F.3d. 1295, 1299 (Fed. Cir. 1999)).

The interpretation of Hansen is of record.

Govindan teaches naked humanized anti-CEA antibodies (MN-14) used to treat cancers [0038, 0045, 0088] and different naked antibody combinations in combination with other therapeutic agents, such as a cytotoxic drug [0088] and antibody doses in the range of 20 to 800 mg/m^2, with doses between 100 and 500 mg/m^2 preferably, for therapy [0092]. The dose range of Govindan is overlapping with the claimed range of 100 to 600 mg.

At the time the invention was made, one skilled in the art would have been motivated and been assured of reasonable success in producing a composition comprising a humanized anti-CEA antibody such as the humanized MN-14 antibody and a therapeutic agent where the antibody dose ranges from 100-600 mg. Griffiths claims the same composition (see Claims 1, 2 and 10 of Griffiths), Hansen specifically discloses and claims a humanized MN-14 antibody having the same binding properties as the murine Mab with reduced immunogenicity and Govindan teaches dose ranges for humanized MN-14 antibody in treating cancer. One skilled in the art would have been assured of success in producing such compositions because both Griffiths, Hansen and Govindan disclose compositions comprising naked humanized anti-CEA antibodies in combination with a therapeutic agent for treating cancer. Griffiths and Govindan show that soluble or unconjugated cytotoxins could be administered in combination with the antibody. Additionally, one skilled in the art would have been motivated and been assured of success in producing the composition because the technology and reagents for producing the components were available at the time the invention was made, and were well known to one of ordinary skill in the art. Thus the claimed compositions were prima facie obvious at the time they were made over Claims 1, 2 and 10 of Griffiths and the disclosures of Hansen and Govindan.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER